Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1-26 (cancelled)

27. (currently amended) A method for designing [[a]] an optimized multi-epitope polypeptide comprising: ~~construct that comprises two or more CTL epitope nucleic acids wherein the construct is presented to an HLA Class I processing pathway, the method comprising steps of:~~

(i) selecting two or more cytotoxic T lymphocyte (CTL) epitopes; and ~~sorting the CTL epitope nucleic acids to minimize the number of junctional epitopes;~~

(ii) incorporating said two or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

(a) ~~introducing~~ a flanking amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitopes; wherein said flanking amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C), and threonine (T); and ~~K, R, N, Q, G, A, S, C, and T at a C+1 position of a CTL epitope nucleic acids;~~

~~(iii)~~ (b) a spacer is introduced between those epitopes of said two or more CTL epitopes that form a junctional epitope when placed adjacent to each other. ~~introducing one or more amino acid spacer residues between two epitope nucleic acids, wherein the spacer prevents the occurrence of a CTL or HTL junctional epitope and~~

~~(iv) selecting one or more multi-epitope constructs that have a minimal number of junctional epitopes, a minimal number of amino acid spacer residues, and a maximum number of K, R, N, G, A, S., C, or T at a C+1 position relative to each CTL epitope nucleic acids.~~

28. (currently amended) A method for designing [[a]] an optimized multi-epitope polypeptide comprising: ~~construct that comprises two or more HTL epitope nucleic acids wherein the construct is presented to an HLA Class II processing pathway, the method comprising steps of:~~

(i) selecting two or more helper T lymphocyte (HTL) epitopes; and ~~sorting said epitope nucleic acids to minimize the number of junctional epitopes;~~

(ii) incorporating said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

(a) ~~introducing~~ a flanking amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking amino acid residue is selected from the group consisting of G, proline (P) [[P]], N or A; and ~~positioned between said nucleic acid epitopes; and~~

~~(iii)~~ (b) a spacer is introduced between those epitopes of said two or more HTL epitopes that form a junctional epitope when placed adjacent to each other. ~~introducing one or more amino acid spacer residues between two epitope nucleic acids, wherein the spacer prevents the occurrence of a HTL junctional epitope.~~

29. (currently amended) The method of claim 28 [[27]], wherein the spacer residues are independently selected from residues that are not known human leukocyte antigen (HLA) [[HLA]] Class II primary anchor residues.

30. (currently amended) The method of claim 28 [[27]], wherein introducing the spacer residues prevents the occurrence of an HTL epitope and further, wherein a spacer comprises at least 5 amino acid residues independently selected from the group consisting of G, P, and N.

31. (currently amended) The method of claim 30, wherein the spacer is GPGPG (SEQ ID NO: 369).

32. (original) The method of claim 27, wherein introducing the spacer residues prevents the occurrence of an HTL epitope and further, wherein the spacer is 1, 2, 3, 4, 5, 6, 7, or 8 amino acid residues selected from the group consisting of A and G.

33. (cancelled)

34. (original) The method of claim 27, wherein the flanking residue is selected from the group consisting of K, R, N, G, and A.

35. (original) The method of claim 27, wherein the flanking residue is adjacent to the spacer amino acid residues.

36. (currently amended) The method of claim 27, further comprising substituting an N-terminal residue of an HLA epitope that is adjacent to a C-terminus of an HLA epitope comprised by the multi-epitope polypeptide ~~construct~~ with a residue selected from the group consisting of K, R, N, G, and A.

37-57 (cancelled)

58. (new) The method of claim 27, further comprising initially sorting the epitopes to be incorporated into the multi-epitope polypeptide to provide an order that minimizes the number of junctional epitopes formed.

59. (new) The method of claim 27, further comprising:

(i) introducing the multi-epitope polypeptide into a cell; and

(ii) determining that the multi-epitope polypeptide is processed by an HLA processing pathway such that all of the epitopes included in the multi-epitope polypeptide are produced by an HLA processing pathway.

60. (new) The method of claim 27, further comprising predicting a structure of said multi-epitope polypeptide.

61. (new) The method of claim 28, further comprising initially sorting the epitopes to be incorporated into the multi-epitope polypeptide to provide an order that minimizes the number of junctional epitopes formed.

62. (new) The method of claim 27, further comprising:

(i) selecting two or more helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

(a) a flanking amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking amino acid residue is selected from the group consisting of G, P, N or A; and

(b) a spacer is introduced between those epitopes of said two or more HTL epitopes that form a junctional epitope when placed adjacent to each other.

63. (new) The method of claim 28, further comprising:

(i) selecting two or more cytotoxic T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

(a) a flanking amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitopes; wherein said flanking amino acid residue is selected from the group consisting of K, R, N, Q, G, A, S, C, and T; and

(b) a spacer is introduced between those epitopes of said two or more CTL epitopes that form a junctional epitope when placed adjacent to each other.

64. (new) The method of claim 27, wherein said multi-epitope polypeptide contains 10 or more CTL epitopes.

65. (new) The method of claim 64, wherein said multi-epitope polypeptide contains 20 or more CTL epitopes.

66. (new) The method of claim 65, wherein said multi-epitope polypeptide contains 30 or more CTL epitopes.

67. (new) The method of claim 66, wherein said multi-epitope polypeptide contains 40 or more CTL epitopes.

68. (new) The method of claim 28, wherein said multi-epitope polypeptide contains 10 or more HTL epitopes.

69. (new) The method of claim 68, wherein said multi-epitope polypeptide contains 20 or more HTL epitopes.

70. (new) The method of claim 69, wherein said multi-epitope polypeptide contains 30 or more HTL epitopes.

71. (new) The method of claim 70, wherein said multi-epitope polypeptide contains 40 or more HTL epitopes.

72. (new) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting two or more cytotoxic T lymphocyte (CTL) epitope nucleic acids; and

(ii) incorporating said two or more CTL epitope nucleic acids into a multi-epitope polynucleotide, wherein, during the incorporation step (ii):

(a) a polynucleotide encoding a flanking amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitope nucleic acids; wherein said flanking amino acid residue is selected from the group consisting of K, R, N, Q, G, A, S, C, and T; and

(b) a polynucleotide encoding a spacer is introduced between those epitopes of said two or more CTL epitope nucleic acids that form a junctional epitope when placed adjacent to each other.

73. (new) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting two or more helper T lymphocyte (HTL) epitope nucleic acids; and

(ii) incorporating said two or more HTL epitope nucleic acids into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

(a) a polynucleotide encoding flanking amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitope nucleic acids; wherein said flanking amino acid residue is selected from the group consisting of G, P, N or A; and

(b) a polynucleotide encoding a spacer is introduced between those epitopes of said two or more HTL epitope nucleic acids that form a junctional epitope when placed adjacent to each other.